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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/578,329

03/12/2007

Olaf Stange

2901652.4

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7590

03/18/2010

Baker Donelson Bearman Caldwell & Berkowitz PC

Att: Docketing Sixth Floor

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Washington, DC 20004

EXAMINER

LE, EMILY M

ART UNIT

PAPER NUMBER

1648

NOTIFICATION DATE

DELIVERY MODE

03/18/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/578,329	Applicant(s) STANGE ET AL.	
	Examiner EMILY M. LE	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2006 and 23 December 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 and 14-20 is/are pending in the application.
- 4a) Of the above claim(s) 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 14-20 is/are rejected.
- 7) ☒ Claim(s) 1-11 and 14-20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/15/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 12/23/2009 is acknowledged. The traversal is on the ground(s) that that Applicant does not agree that the groups of inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1. Applicant also cited *In re Ochiai* guidelines in asserting that the method and product should be allowed together in the same application. This is not found persuasive because it is found that the inventions listed as Group I and Group II lack a single general inventive concept. As discussed in the requirement itself, the general concept shared between the two groups is not a general inventive concept for the technical feature shared between the two groups is not a shared special technical feature as the feature fails to provide a contribution over the cited art. Regarding Applicant's other argument, Applicant is correct to note that method and product should be allowed in the same application. As evidenced by the claims of the instant patent applicant, which contains method and product claims when the application was filed. In the instant case, restriction/lack of unity requirement between the inventions is proper for the listed inventions lack unity with the other. Additionally, in accordance with *In re Ochiai* and as detailed in the requirement, Applicant would have been entitled to a rejoinder of withdrawn process claims that depend from or otherwise require all the limitation of the elected and allowable product. However, in the instant case, Applicant did not elect the product, rather elected the method instead, so rejoinder practice under *In re Ochiai* is not applicable.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

2. Claim 13 is cancelled. Claims 1-12 and 14-20 are pending. Claim 12 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/23/2009. Claims 1-11 and 14-20 are under examination.

Claim Objections

3. Claims 1-11 and 14-20 are objected to because of the following informalities: Insertion of "and) between steps b) and c) in independent claim 1 is necessary. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-11 and 14-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 1, which claims 2-11 and 14-20 depend, requires the cooling of the mixture, however, it is unclear how cooling can take place when the claimed method does not require the phases or resulting emulsion to be heated.

Claim 6 requires the emulsification in step a) to be carried out at 30-35 degrees Celsius. However, step a), as presented, is not an emulsification step. Step a) simply

directed at the stirring of active ingredients into the aqueous phase. For the purpose of examination, the Office interprets the claim to be directed at the emulsification of step b).

Claim 19 recites the limitation "said peptide" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-10 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higashi et al.,¹ in view of Joscelyne et al.,² and Moeritz, M.,³ in further view of Forster et al.,⁴

The claims are directed a process for the preparation of a multiple emulsions that comprises on or more active ingredients, the method comprises a) stirring active ingredient into an aqueous phase, b) emulsifying the aqueous phase by passing the aqueous phase through a largepored, porous membrane into an oil phase, and c) cooling the mixture at a cooling rate of at least .3K/min, thereby causing phase inversion

¹ Higashi et al. Size of lipid microdroplets effects results of hepatic arterial chemotherapy with an anticancer agent in water-in-oil-in-water emulsion to hepatocellular carcinoma. The Journal of Pharmacology and Experimental Therapeutics, 1999, Vol. 289, No. 2, 816-819.

² Joscelyne et al. Membrane emulsification—a literature review. Journal of Membrane Science, 2000, Vol. 169, 107-117.

³ Moeritz, MI. DE 19630176, published 01/29/1998, which is provided by Applicant on 08/15/2006 IDS.

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of the emulsion and wherein an emulsifier is added either to the aqueous phase in a) or the oil phase in b) or both phases. Claim 2, which depends on claim 1, requires the membrane to be a porous inorganic membrane. Claim 3, which depends on claim 1, requires the membrane to be .2-.5 μm in size. Claim 4, which depends on claim 1, requires the oil to be mineral oil, white oil or vegetable oil. Claim 5, which depends on claim 1, requires the emulsifier to be a nonionic emulsifier and added to the oil phase. Claim 6, which depends on claim 1, requires step a) to be carried out at 30-35 degrees Celsius. Claim 7, which depends on claim 1, requires the phase inversion of step c) to be carried out at a cooling rate of at least 1 K/min. Claim 8, which depends on claim 1, requires the pressure difference over the membrane be $.5 \times 10^5$ Pa to 25×10^5 Pa. Claim 9, which depends on claim 1, requires the process to be carried out continuously in all steps. Claim 10, which depends on claim 1, requires the active ingredient to be a pharmaceutical active ingredient. Claim 14, which depends on claim 1, requires the membrane to be a ceramic membrane. Claim 15, which depends on claim 14, requires the ceramic membrane to comprise of aluminum oxide, zirconium oxide and/or titanium oxide. Claim 16, which depends on claim 1, requires the pore size of the membrane to be .3 to 3 μm . Claim 17, which depends on claim 10, requires the active ingredient to be appropriate for veterinary uses.

Higashi et al. teaches a process for the preparation of a multiple emulsions that comprises on or more active ingredients, the method comprises first making a single W/O emulsion, and then using that first W/O emulsion to create the multiple emulsion.

⁴ Forster et al. Production of fine disperse and long-term stable oil-in-water emulsion by the phase

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[Experimental Procedures, in particular.] To make the W/O emulsion, Higashi et al. stirred the a) active ingredient into an aqueous phase and b) emulsifying the aqueous phase into an oil phase by the conventional technique of sonication to make the W/O emulsion. Higashi et al. then prepared the multiple emulsion using the membrane emulsification method, which requires passing the W/O emulsion through a largepored, porous membrane into an aqueous phase. Higashi et al. uses polyoxyethylene(40) hydrogenated castor oil as the emulsifier, a non-ionic surfactant added to the oil phase. The oil used by Higashi et al. is poppy seed oil, a vegetable oil. The active ingredient used by Higashi et al. is epirubicin, a pharmaceutical active ingredient, which may be appropriate for veterinary uses.

Higashi et al. did not create W/O emulsion by emulsifying the aqueous phase by passing the aqueous phase through a largepored, porous membrane into an oil phase. However, at the time the invention was made, Joscelyne et al. teaches a process for making W/O emulsion by emulsifying the aqueous phase by passing the aqueous phase through a largepored, porous membrane into an oil phase. [Introduction section, page 107, in particular.] Joscelyne et al. teaches that such emulsification technique is highly attractive given its simplicity, potentially lower energy demands, need for less surfactant and the resulting narrow droplet size distribution compared to conventional techniques.

Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use the emulsification technique of

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Joscelyne et al. to make the W/O emulsion of Higashi et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so because the membrane emulsification technique is simple, potentially have lower energy demands, need for less surfactant and the resulting narrow droplet size distribution compared to conventional techniques. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because Joscelyne et al. discloses the use of membrane emulsification technique to make W/O emulsions.

The membrane disclosed by Joscelyne et al. is a porous inorganic membrane including ceramic membrane comprising aluminum oxide, zirconium oxide and/or titanium oxide. [Paragraph bridging columns, page 109, in particular.] Joscelyne et al. teaches that these membranes typically have pore size ranging from .05-14 μm .

Neither Higashi et al. nor Joscelyne et al. teach phase inversion of the W/O to make W/O/W by cooling the mixture. However, at the time the invention was made, Moeritz, M. teaches the use of phase inversion of W/O to make W/O/W emulsions. The technique of Moeritz, M. comprises heating and cooling the emulsion. In the instant case, Moeritz, M. teaches an alternative technique to making W/O/W emulsions. It would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to use the phase inversion technique of Moeritz, M. as an alternative to the membrane emulsification technique of Higashi et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so

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to make W/O/W emulsion. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of alternative protocols is routinely practiced in the art.

Regarding claim 6, Higashi et al., Joscelyne et al. and Moeritz, M. do not teach that the formation of the W/O emulsion be carried out 30-35 degrees Celsius. However, Joscelyne et al. discloses that temperature can be an important parameter in emulsification affecting both the viscosity of the dispersed and continuous phases and also the nature of the emulsifier as a consequence of phase inversion temperature. [Section 3.5, in particular.] Joscelyne et al. notes that emulsification temperature usually dictated by the requirements of a product. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to vary the emulsification temperature. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to optimize the emulsification conditions. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

Regarding claim 8, Higashi et al., Joscelyne et al. and Moeritz, M. do not teach that the pressure difference over the membrane be $.5 \times 10^5$ Pa to 25×10^5 Pa. However, Joscelyne et al. discloses that pressure difference over the membrane is a result effective variable. Joscelyne et al. discloses that such pressure is dependent on the membrane pore diameter, oil/water interfacial tension and the contact angle between the dispersed phase and membrane surface. Thus, at the time the invention

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was made, it would have been prima facie obvious for one of ordinary skill in the art to vary the pressure difference over the membrane. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to optimize the emulsification conditions. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

Regarding claim 9, Higashi et al., Joscelyne et al. and Moeritz, M. do not teach that the entire W/O/W process be continuously carried out. However, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to have carried out the claimed invention continuously. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to optimize and streamline the production of W/O/W emulsions comprising active ingredients. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because optimize and streamlining production methods are routinely practiced in the art.

Regarding the limitations directed at the cooling rates of at least .3K/min and at least 1K/min, Higashi et al., Joscelyne et al. and Moeritz, M. do not teach the claimed cooling rate. However, at the time the invention was made, Forster et al. establishes that the influence of cooling rate in phase inversion using the temperature technique is insignificant. [First full paragraph, page 190, in particular.] Hence, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use various cooling rate. One of ordinary skill in the art, at the time the

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invention was made, would have been motivated to do so optimize the cooling of the emulsion. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

8. Claims 1, 10-11 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higashi et al., in view of Joscelyne et al., Moeritz, M., and Forster et al., as applied to claims 1 and 10, in further view of Ganne, V.⁵

Claim 11, which depends on claim 10, requires the active ingredient to comprise an antigen. Claim 18, which depends on claim 10, requires the active ingredient to comprise an antigen for a vaccine formulation. Claim 19, which depends on claim 11, requires the antigen to comprise a virus, or a microorganism. Claim 20, which depends on claim 10, requires the active ingredients to comprise at least one of the bacterium, a parasite, a glycoprotein that has been obtained from microorganism, a synthetic peptide, and/or a protein or peptide which has been prepared by genetic manipulation.

Higashi et al., Joscelyne et al., Moeritz, M., and Forster et al. does not teach an active ingredient that is encompassed by claims 11 and 18-20. However, at the time the invention was made, Ganne, V. teaches of active ingredients encompassed by claims 11 and 18-20. Ganne, V. teaches the inclusion of an antigen such as a virus, a microorganism, bacterium, parasite or compounds comprising peptide chain, such as protein or glycoprotein obtained from a microorganism, synthetic peptide or a protein or a peptide obtained by genetic engineering. In the instant case, Ganne, V. teaches the

⁵ Ganne et al. U.S. Patent No. 6251407, published June 26, 2001.

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inclusion of said active ingredients in an emulsion to facilitate its delivery. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use the active ingredients of Ganne, V in the emulsion of Higashi et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to facilitate the delivery of the active ingredient. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the substitution one active ingredient with another is routinely practiced in the art.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick J. Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/EMILY M LE/
Primary Examiner, Art Unit 1648

/E. M. L./
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